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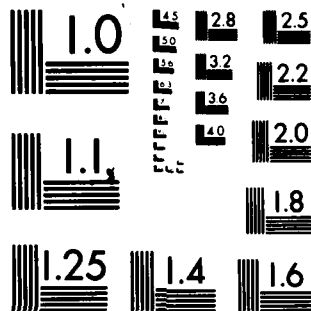
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Report Number 1

RELATIONSHIP OF ANUG, STRESS, AND LEUKOCYTE FUNCTION

ANNUAL SUMMARY REPORT

Ronald B. Cogen, Alvin W. Stevens,  
Steven Cohen-Cole and Katherine Kirk

October 15, 1980

Supported by

U. S. ARMY MEDICAL RESEARCH AND DEVELOPMENT COMMAND  
Fort Detrick, Frederick, Maryland 21701

Contract No. DAMD 17-79-C-9176

University of Alabama School of Dentistry  
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20. ABSTRACT (Continue on reverse side if necessary and identify by block number) Our first year in the study has thus far resulted in some important findings. The ANUG patients appear to be suffering from anxiety which may be correlated by a tendency for an increase in serum cortisol, and an increase in urine cortisol. Also it appears as though increased susceptibility to the microorganisms may be based on decreased lymphocyte and PMN function.		



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Summary:

Our first year in the study has thus far resulted in some important findings. The ANUG patients appear to be suffering from anxiety which may be correlated by a tendency for an increase in serum cortisol, and an increase in urine cortisol. Also it appears as though increased susceptibility to the microorganisms may be based on decreased lymphocyte and PMN function.

Foreward:

This is the first annual report, and I am happy to report that we have been able to exceed our first year milestone of 35 patients. In fact, we have seen over 40 patients in the first year of the study. We have been accumulating a wealth of data and analysis of this data has been encouraging that we are on the right track. It also is suggesting some new avenues for further investigation which may prove fruitful in our understanding not only of ANUG, but also other stress-related diseases and host-related defense mechanisms.

Body of Report:

Some of our findings to date are as follows:

- (1) Most of the patients were between 17-23 years of age. The youngest patient was 14 years old and the oldest was 28 years old.
- (2) All of the patients with ANUG with the exception of one were caucasian. This suggests that there may be a genetic component and may be worth investigating. We feel that this may be an important uncovered component and was an unexpected finding.
- (3) The differential white blood cell counts were within the normal range for all patients as well as controls.
- (4) The data from the psychologic testing instruments suggests:
  - (a) General Health Questionnaire - on the first visit the ANUG patients score 8.3 vs. 3.6 for the controls with a  $P=0.0006$  indicating that this is highly significant. On the two week follow-up visit, the patients scored 5.0 and the controls scored 3.4 - the  $P=0.28$  suggests that the difference is not significant and the drop from 8.3 to 5.0 in patients' scores suggests that the ANUG contributed to the higher scores on the first visit. However past experience with use of this instrument suggests that a score of 5.0 or above is taken to mean that a patient is psychologically disturbed - so that there is a trend which may be significant when one compares the number of patients that are scoring 5.0 or higher when compared to controls.
  - (b) Data from Social Support instruments suggests a trend for decreased social support in the ANUG patients. On the first visit the patients'

score of -1.00 compared to control scores of +1.23 is significant at the  $P=0.10$  level. Again on the second or follow-up visit, patients score of -0.36 compared to control scores of +0.45 is not statistically significant,  $P=0.55$ , however it appears that there is unquestionably a trend which may require larger sample to prove significant.

- (c) Mood Test data indicates that on the first visit ANUG patients are scoring 18 compared to 11 for controls, this difference in mood is significant  $P=0.008$ . On the return visit the difference is lessened with patients scoring 13 and controls 10 and is insignificant  $P=0.3$ . This indicates that the disease appears to be contributing significantly to their feelings and resolution of disease improves patient outlook or mood. However, when scored for depression, ANUG patients show significantly more depression on both first and follow-up visits,  $P=0.03$ .
  - (d)
    - 1. Test for State Anxiety indicates that patients with ANUG definitely were experiencing anxiety. On the first visit, ANUG patients are scoring 47.97 and controls are scoring 36.17 and  $P=0.0001$ . On the second visit, ANUG patients are scoring 45.5 compared to 36.7 for controls - the difference again is significant  $P=0.0001$ . There is no significant change in pre-op compared to post-op scores in either the ANUG patients or the control. This indicates that the ANUG patients were experiencing anxiety (stress) which was not caused by presence of the disease (ANUG).
    - 2. Trait Anxiety testing indicated that on the first visit ANUG patients scored 46.9 compared to 38.2,  $P=0.0001$ . However, on the second visit ANUG patient scores dropped to 41.9 and controls did not change scoring 37.7 - the  $P=0.19$  suggested that this difference was not significant. This data was interpreted to mean that ANUG patients showed no more trait toward anxiety than the controls, and that they were more anxious due to life events.
  - (e) The data from the Minnesota Multiphasic Personality Inventory (MMPI) has not been completely tabulated. However, the scoring of ANUG patients has suggested interesting results based on visual observation of the data. That is that many, possibly a clear preponderance of the ANUG patients demonstrate clear evidence of severe psychopathology.
- (5) Urinary levels of Endocrine Markers of stress
- (a) There is no significant difference in levels of catecholamine excretion in ANUG patients compared to controls in either first or second visits.
  - (b) Urine cortisol levels indicate that on the first visit, ANUG patients are excreting 91.2 mg cortisol/gm creatinine compared to 71.2 mg cortisol/gm creatinine for controls,  $P=0.1$ . If not significant, this at least shows a trend. It is important to note that these values were calculated on the basis of overnight samples, and unfortunately included some spot samples. We are now in the process of

separating these and recalculating the values. In addition, on the second visit ANUG patients are excreting 67.01 mg cortisol/gm creatinine compared to control levels of 44.06 mg cortisol/gm creatinine,  $P=0.05$ . This difference is significant and is based only on overnight samples. The trend for increased urine cortisol on the first visit and the significantly increased level on the second visit, corroborate the results of the Stait Anxiety test.

- (6) Serum levels of Endocrine Markers of stress are not as clear-cut. All hormone concentrations were within the normal range in both groups and there was no statistical difference in values for T3, T4, T3:T4, prolactin or growth hormone. Plasma cortisol levels shows a tendency to be higher in ANUG patients - mean 20.4 ug/dl, when compared to controls - mean 16.9 ug/dl,  $P=0.10$ . This tendency of increased plasma cortisol levels in ANUG patients further corroborates the increased urine levels and the psychologic anxiety of the patients.
- (7) Blood leukocyte function assays yield interesting data regarding possible pathogenic mechanisms in ANUG.
  - (a) Lymphocyte function as measured by stimulation by mitogens
    1. Phytohemagglutinin (PHA) stimulation assay indicates that 70.3% of ANUG patients have a decreased response compared to controls,  $P=0.28$ . This suggests that there is a trend but also that it is not a statistically significant decrease in response.
    2. Concanavallin A (Con A) stimulation assay indicates that 90.0% of the ANUG patients have a decreased response compared to controls,  $P=0.0002$ . This suggests that this decrease is highly significant.
  - (b) Polymorphonuclear (PMN) function as measured by leukotaxis indicates that 85.0% of the ANUG patients have decreased leukotaxis when compared to controls,  $P=0.0006$ . This decrease in response to chemotactic stimulation is highly significant.
  - (c) PMN function as measured by phagocytosis is similarly indicated that 85.0% of ANUG patients have a decrease in phagocytic capability of their PMN,  $P=0.0006$ . This decrease in phagocytosis is again highly significant.